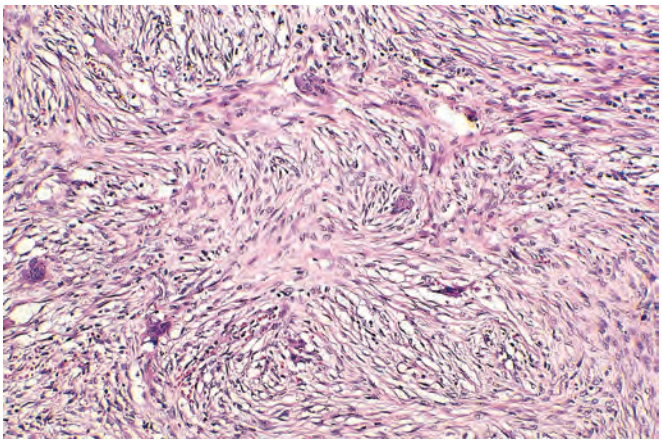

Figure 26-37 Storiform pattern created by benign spindle cells with scattered osteoclast-type giant cells characteristic of a fibrous cortical defect and nonossifying fibroma.

Fibrous Dysplasia

Fibrous dysplasia is a benign tumor that has been likened to a localized developmental arrest; all of the components of normal bone are present, but they do not differentiate into mature structures. The lesions arise during skeletal development, and appear in several distinctive but sometimes overlapping clinical patterns:

- Monostotic: involvement of a single bone
- Polyostotic: involvement of multiple bones
- *Mazabraud syndrome*: fibrous dysplasia (usually polyostotic) and soft tissue myxomas
- *McCune-Albright syndrome*: polyostotic disease, associated with café-au-lait skin pigmentations and endocrine abnormalities, especially precocious puberty.

Pathogenesis. All of the above manifestations result from a somatic gain-of-function mutation during development in *GNAS1*, the gene that is also mutated in pituitary adenomas (Chapter 24). The mutations produce a constitutively active G_s-protein that promotes cellular proliferation. The extent of phenotype depends on (1) the stage of embryogenesis when the mutation is acquired and (2) the fate of the cell harboring the mutation. At one extreme, a mutation during embryogenesis produces the McCune-Albright syndrome while a mutation in an osteoblast precursor, during or after formation of the skeleton, results in monostotic fibrous dysplasia. The skeletal manifestations arise from G_s-cAMP mediated interruption of normal osteoblast differentiation from precursors.

MORPHOLOGY

The lesions of fibrous dysplasia are well circumscribed, intramedullary, and vary greatly in size. Larger lesions expand and distort the bone. The lesional tissue is tan-white and gritty and is composed of curvilinear trabeculae of woven bone surrounded by a moderately cellular fibroblastic proliferation. The curvilinear shapes of the trabeculae mimic Chinese characters, and the bone lacks prominent osteoblastic rimming (Fig. 26-38). Nodules of hyaline cartilage with the appearance of disorganized growth plate are also present in approximately 20% of cases. Cystic degeneration, hemorrhage, and foamy macrophages are other common findings.

Clinical Course. Monostotic fibrous dysplasia occurs equally in boys and girls, usually in early adolescence, and often stops enlarging at the time of growth plate closure. The femur, tibia, ribs, jawbones, calvarium, and humerus are most commonly affected. The lesion is frequently asymptomatic and usually discovered incidentally but it may cause pain, fracture, and discrepancies in limb length. The lesion is readily recognized radiologically by its typical ground-glass appearance and well-defined margination. Symptomatic lesions are cured by curettage.

Polyostotic fibrous dysplasia manifests at a slightly earlier age than the monostotic type and may continue to cause problems into adulthood. The bones affected, in descending order of frequency, are the femur, skull, tibia, humerus, ribs, fibula, radius, ulna, mandible, and vertebrae. Craniofacial involvement is present in 50% of those who have a moderate number of bones affected and in 100% of those with extensive skeletal disease. Polyostotic disease has a propensity to involve the shoulder and pelvic girdles, resulting in severe, progressive disease including crippling deformities and fractures. Patients may require multiple corrective orthopedic surgical procedures. Bisphosphonates can be used to reduce the severity of the bone pain. A rare complication, usually in the setting of polyostotic involvement, is malignant transformation of a lesion into a sarcoma.

Mazabraud syndrome presents with skeletal features of polyostotic fibrous dysplasia with multiple skeletal deformities identified in childhood. The intramuscular myxomas present in adulthood often in the same anatomic region as existing fibrous dysplasia. Although benign, these tumors can cause local compression symptoms or further deformity to a limb but are cured by surgical excision.

The most common clinical presentation of *McCune-Albright syndrome* is precocious sexual development, which occurs most often in girls. The syndrome can include other endocrinopathies such as hyperthyroidism, pituitary adenomas that secrete growth hormone, and primary adrenal hyperplasia. The bone lesions are often unilateral, and the skin pigmentation is usually limited to the same side of the body. The cutaneous macules are classically large; dark to

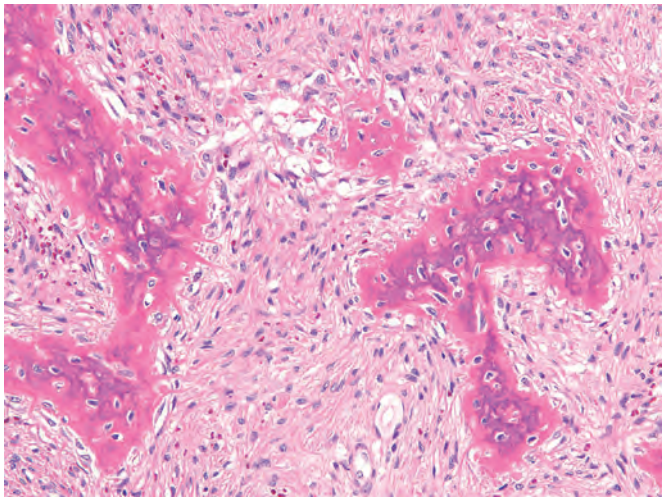

Figure 26-38 Fibrous dysplasia composed of curvilinear trabeculae of woven bone that lack conspicuous osteoblastic rimming and arise in a background of fibrous tissue.